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Anion recognition by phosphonium calix[4]arenes: synthesis and physico-chemical studies

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p-tert-Butylcalix[4]arenes, in the cone conformation, di- and tetra-substituted at the narrow rim with charged phosphonium groups, have been synthesised and characterised. Their interactions with a wide range of anions have been investigated in chloroform and acetonitrile solutions by means of ^{1}H and ^{31}P NMR and isothermal titration microcalorimetry. These compounds have also been incorporated as sensing material in poly(vinyl chloride) ion-selective electrodes. The results showed that they interact strongly with the more lipophilic anions ClO_4^-, SCN^- and I^-, in solution as in the electrode membranes. The origin of this selectivity is discussed and, in particular, the role of the salt counterion is examined.

Keywords: phosphonium calix[4]arenes; anion binding properties; microcalorimetry; ion-selective electrodes

Introduction

Anions play an important role in many biological processes, such as regulation of cell activity, synthesis of proteins and transport of hormones (*1–3*). They are also frequently used in many industrial technologies, which very often generate an increase of the concentration of anions in the environment or even introduce anionic species which were unknown so far in ecosystems. The presence of these anions is crucial in environmental and medical concerns, as they are pollutants and may have harmful effects on living organisms and human health (*4–6*). Therefore, there is a need of fast and selective anion detection methods allowing real-time monitoring of anion concentration changes and of efficient clean up processes. Design of anion receptors for such applications remains a great challenge for chemists because they have to take into consideration the specific anion properties, such as a large range of shapes and geometries, small electric charges vs. sizes, high free energies of solvation and, in some cases, multiple oxidation states of the central atoms in oxoanions or pH dependence. In many artificial anion hosts, non-covalent interactions are responsible for host–guest recognition. They include electrostatic interactions, hydrogen bonding, hydrophobic effects and coordination to a metal ion or combinations of these interactions. The hosts can be neutral, containing urea (*7–10*), thiourea (*11*, *12*) or amide functions (*13*). They can also be positively charged, containing pyridinium (*14*), polyammonium (*15*) or quaternary ammonium (*16*) binding sites. Calix[4]arenes (*17*, *18*) and porphyrins (*19*) are often used as scaffolds into which these functional groups can be grafted. Calixpyrroles are also known as efficient anion receptors (*20*, *21*).

Recently, we described the synthesis and characterisation of a new calix[4]arene derivative (**5**) bearing four positively charged triphenyl phosphonium groups (*22*). The presence of these highly polarisable moieties, where the charge is spread over the three aromatic rings, was expected to favour the interaction with lipophilic anions. Preliminary binding studies showed that this ligand interacted selectively with some anions, namely ClO_4^- and SCN^-. This compound was also incorporated, as ionophore-sensing material, in ion-selective electrodes (ISEs) which exhibited a selectivity order similar to the Hofmeister series. The disubstituted derivative **1** was also synthesised as the hexafluorophosphate (*23*).

In order to get more information on the mechanisms involved in the recognition process and to optimise its selectivity, we have now extended this study to new di- and tetra-substituted phosphonium calix[4]arene derivatives (compounds **2**–**4**, **6** and **7**) and re-examined the properties of **1** and **5** (Figure 1). In some of these compounds, one of the phenyl rings on the phosphonium groups has been replaced by a methyl radical or a hydrogen atom. The presence of such small substituents is expected to increase the charge density on the phosphorus atoms and their accessibility (*24*). Moreover, the presence of hydrogen atoms may induce the formation of hydrogen bonds with anions. The possibility of tuning the charge density on the phosphorus atoms by changing the nature of their substituents could allow the design of receptors able to distinguish lipophilic anions such as ClO_4^-, SCN^-, I^- or NO_3^- from other anions and between them. The

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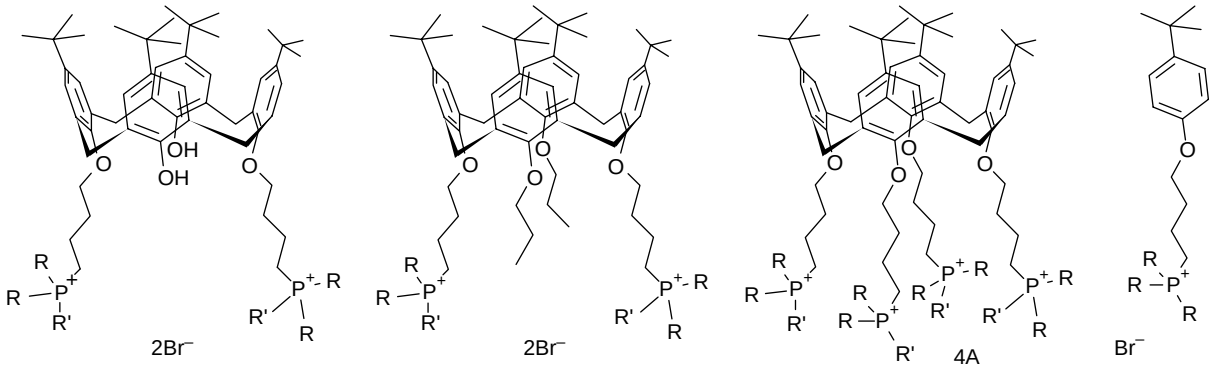


1: R, R' = Ph
2: R = Ph, R' = Me

3: R, R' = Ph
4: R = Ph, R' = Me

5: R, R' = Ph, A = Br^-
5a: R, R' = Ph, A = ClO_4^-
5b: R, R' = Ph, A = PF_6^-

6: R = Ph R' = Me, A = Br^-
6a: R = Ph R' = Me, A = ClO_4^-
6b: R = Ph R' = Me, A = PF_6^-

7: R = Ph R' = H, A = Br^-

8: R = Ph

Figure 1. Chemical structures of the ligands under study.

binding properties of these compounds towards a variety of anions have been followed by ^1H and ^{31}P NMR and by isothermal titration microcalorimetry. In particular, the role of the salt counterion was examined using these techniques.

Results and discussion

Synthesis

The ligands synthesised in this work (Figure 1) are based on a tetrakis-*p-tert*-butylcalix[4]arene platform which presents several advantages. It has a well-defined size and is readily amenable to substitution at its lower rim where ligating groups can be attached and in some extent pre-organised. The amphiphilicity of such derivatives should allow their introduction into the membranes of ISEs.

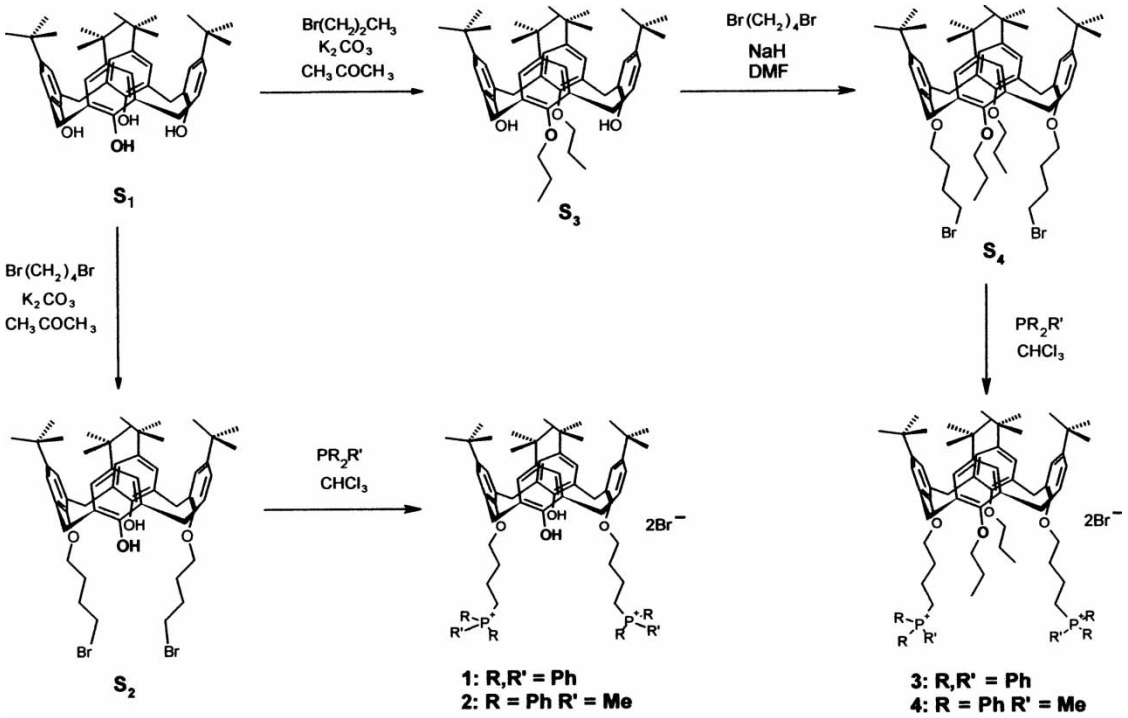
Diphosphonium ligands were synthesised in two or three steps according to the known procedure (*23*). The first step was the selective bromoalkylation of the tetrakis-*p-tert*-butylcalix[4]arene ($\mathbf{S_1}$), leading to the intermediate molecules $\mathbf{S_2}$ or $\mathbf{S_3}$ in 71 and 55% yield, respectively (Scheme 1). 1,3-Bis-(4-triphenylphosphonium-butoxy)-*p-tert*-butyl-calix[4]arene dibromide (**1**) was obtained by the reaction of $\mathbf{S_2}$ with 10 equivalents of triphenylphosphine. After 6 days under reflux in chloroform, the product was precipitated from a dichloromethane–hexane mixture in 76% yield. 1,3-Bis-(4-(*P,P*-diphenyl-*P*-methylphosphonium)-butoxy)-*p-tert*-butylcalix[4]arene dibromide (**2**) was obtained during the reaction of $\mathbf{S_2}$ with 10 equivalents of diphenylmethylphosphine in the same conditions in 69% yield.

The more lipophilic molecules **3** and **4**, where the free phenolic protons are substituted with propyl groups, were prepared in order to increase their stability in the lipophilic membrane of ISEs. The reaction of $\mathbf{S_3}$ with 10 equivalents of 1,4-dibromobutyl, refluxed for 4 days in dimethylformamide in the presence of 7 equivalents of NaH, gave 1,3-bis-(propoxy)-2,4-bis-(butoxy-4-bromide)-tetrakis-*p-tert*-butylcalix[4]arene ($\mathbf{S_4}$) in 57% yield. Compounds **3** and **4** were obtained by the reaction of $\mathbf{S_4}$ with 10 equivalents of triphenylphosphine and 10 equivalents of diphenylmethylphosphine in chloroform in 76 and 64% yield, respectively (Scheme 1).

Tetraphosphonium ligands **6** and **7** were synthesised according to the procedure already described for **5** (*22*) from the intermediate molecule tetrakis-(butoxy-4-bromide)-*p-tert*-butylcalix[4]arene ($\mathbf{S_5}$) by substitution of the bromine atoms of the alkyl chains (Scheme 2). The tetrakis-(4-(*P,P*-diphenyl-*P*-methylphosphonium)-butoxy)-*p-tert*-butylcalix[4]arene tetrabromide (**6**) was obtained from the reaction of $\mathbf{S_5}$ with 20 equivalents of diphenylmethylphosphine in chloroform in 59% yield.

Ligand **7** was synthesised in three steps. The reaction of $\mathbf{S_5}$ with 5 equivalents of $KPPh_2$ gave the product $\mathbf{S_6}$ in 40% yield (*25–27*). $\mathbf{S_6}$ was then protonated with an excess of HBr giving ligand **7** in 52% yield.

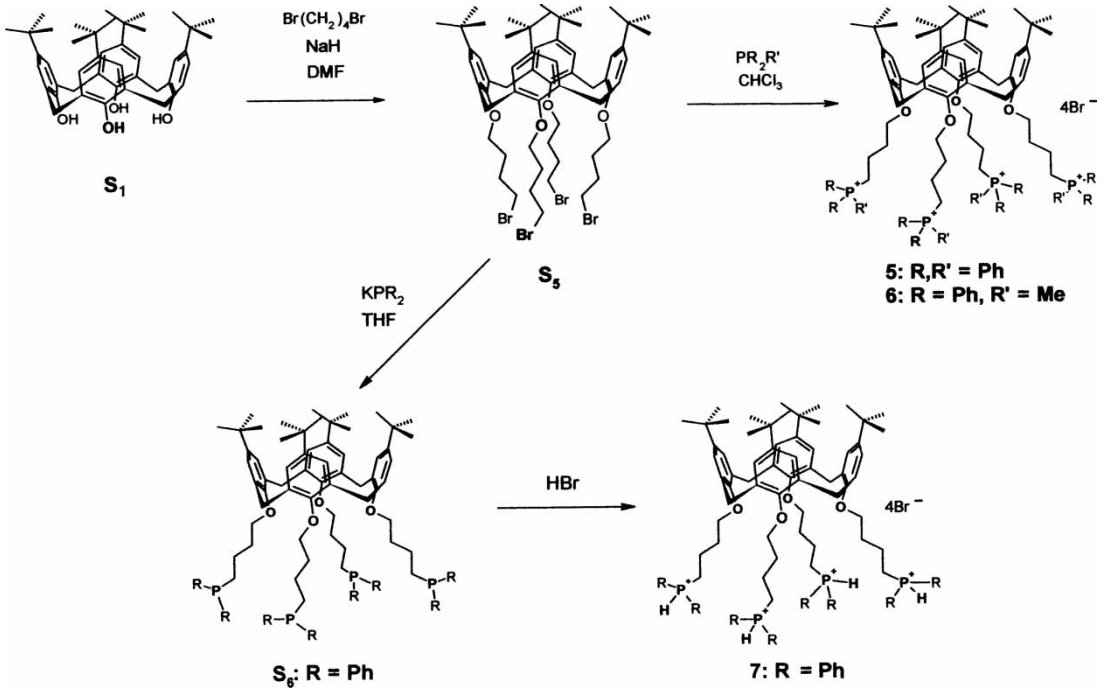
In order to study the influence of the ligand counterion on the ligand–anion interactions, the tetra-substituted phosphonium ligands were also synthesised as perchlorates (**5a** and **6a**) and hexafluorophosphates (**5b** and **6b**). These compounds were obtained by the reaction of ligands **5** and **6** with the appropriate silver salts.



Scheme 1. Synthesis of diphosphonium ligands.

For comparison purpose, the monomeric subunit of ligand **5**, triphenylphosphonium-butoxy-*p*-*tert*-butylphenol bromide (**8**), was synthesised as previously described (*22*).

The cone conformation of the disubstituted calix[4]-arenes was indicated by their presence in the ^{1}H NMR spectra of two singlets for the *tert*-butyl protons (at 0.99 and 1.28 ppm for **1** and 0.96 and 1.29 ppm for **2**) and an AB system for the methylene protons (at 3.19 and 3.90 ppm for **1** and at 3.23 and 4.02 ppm for **2**). The ^{1}H NMR spectra of ligands **5** and **6** are characteristic of tetra-substituted derivatives of calix[4]arenes in the cone conformation. For instance, in the case of **6**, it is indicated by the presence of



Scheme 2. Synthesis of tetraphosphonium ligands.

the singlet corresponding to the protons of the *tert*-butyl groups at 1.03 ppm and the AB system of the methylene protons of the calixarene at 4.26 and 3.03 ppm. Two well-defined multiplets for the protons of the aromatic phosphonium groups can be observed as well as one doublet for the methyl protons in the direct neighbourhood of the phosphorus atoms.

The spectrum of the protonated phosphonium ligand **7** presents several broad peaks corresponding to multiplets in coalescence. Only two singlets could be clearly observed, one for the *tert*-butyl groups and one for the aromatic protons of the calix[4]arene, suggesting also the cone conformation of this molecule.

Binding studies

^{1}H and ^{31}P NMR studies in chloroform

The interactions between the phosphonium calixarenes and the anions NO_3^-, ClO_4^-, I^-, SCN^-, SO_4^{2-}, HCO_3^- and $Cr_2O_7^{2-}$ provided as sodium salts were studied by ^{1}H and ^{31}P NMR in $CDCl_3$. Among these anions, only perchlorate, thiocyanate and iodide salts induced changes in the ^{1}H NMR spectra of the ligands. The changes observed in the case of the disubstituted ligand **1** upon addition of sodium perchlorate are illustrated in Figure 2. The main signals affected were those of the CH_2 protons (i,j) directly bound to the carbon atoms next to the phosphorus atoms and the aromatic protons (k) of the phosphonium groups (see Table S1, Supplementary Material). The shifts of these signals due to changes in the charge density on the phosphorus atoms reflect interactions with these anions.

Similar but smaller changes were induced in the spectrum of ligand **2** by the presence of the same anions (see Table S2, Supplementary Material). As with ligand **1**, no change is observed for the aromatic protons (c,d) and for the protons (e,f) of the methylene bridge, indicating that the conformation of the calixarene unit is not disturbed. This may be explained by the high rigidity of these disubstituted derivatives due to hydrogen bonds involving free phenolic groups.

In the ^{31}P NMR spectra of the free ligands **1** and **2**, and of these ligands in the presence of sodium iodide, thiocyanate and perchlorate, the phosphorus atoms appear as a singlet indicating that the two phosphonium groups are chemically equivalent and participate in the anion–ligand interaction. The most important changes in chemical shifts are observed for perchlorate: $\Delta\delta = 0.602$ and 0.620 ppm with **1** and **2**, respectively (Table 1).

With the tetra-substituted calix[4]arene **5** previously studied (*22*) and ClO_4^-, SCN^- and I^-, the most important changes in chemical shifts corresponded to the signals of the methylene bridge protons and the aromatic protons of the calixarene, indicating changes in the conformational tensions of the calixarene scaffold. The signals corresponding to protons of the butyl chains were also shifted as well as the aromatic protons of the phosphonium. On the contrary, no change was observed with monomer **8** (*22*).

The spectrum of ligand **6** was also modified in the presence of these anions (see Table S3, Supplementary Material). In particular, the signals corresponding to the protons of the calix[4]arene scaffold are shifted in a comparable way for the three anions. The changes observed

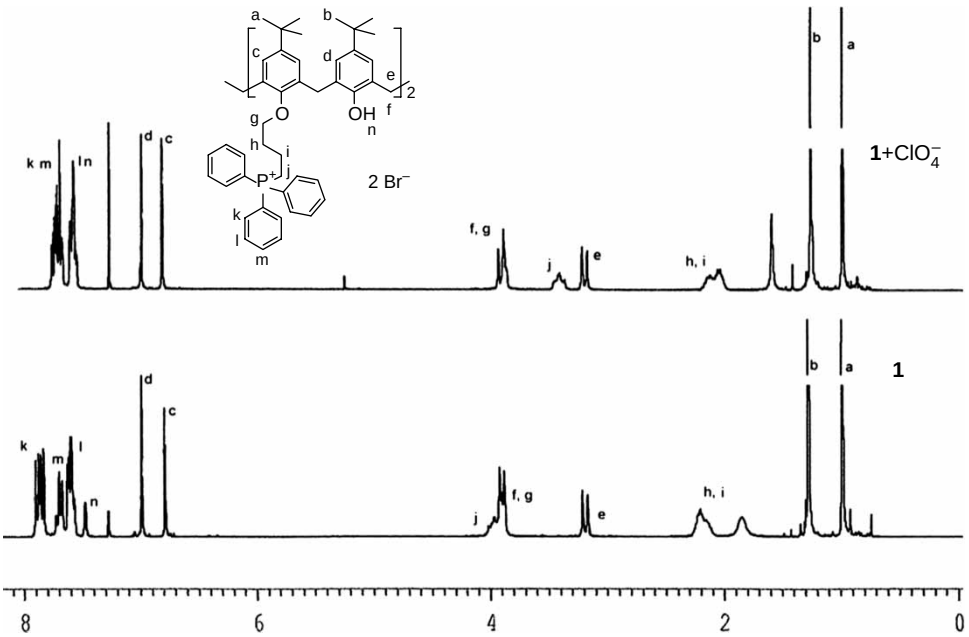


Figure 2. ^{1}H NMR spectra of ligand **1** alone and in the presence of ClO_4^- in $CDCl_3$.

Table 1. Changes ($\Delta\delta$ in ppm) in the ^{31}P NMR spectra of phosphonium ligands in the presence of sodium iodide, thiocyanate and perchlorate in $CDCl_3$.

	1	**2**	**5**	**6**
Ligand (δ)	25.797	25.962	25.756	25.982
Ligand+I^- ($\Delta\delta$)	0.215	0.203	0.210	0.175
Ligand+SCN^- ($\Delta\delta$)	0.470	0.530	0.767	0.965
Ligand+ClO_4^- ($\Delta\delta$)	0.602	0.620	0.992	1.170

in the spectrum of this ligand in the presence of ClO_4^- are illustrated in Figure 3.

With this anion, the multiplets corresponding to the protons (g) and (j) from 3.87 to 3.70 ppm give two multiplets from 4.36 to 4.17 ppm for (g) and from 3.28 to 3.11 ppm for (j). The multiplet from 8.17 to 8.02 ppm for proton (k) is shifted upfield and gives one multiplet from 7.90 to 7.70 ppm, whereas the multiplet from 7.78 to 7.54 ppm of protons (l,m) does not move significantly. The doublet of the CH_3 protons (o) adjacent to the phosphorus atoms at 2.91 ppm is strongly shifted to 2.50 ppm.

The addition of the anions studied to **7** does not induce any change in its ^{1}H NMR spectrum. Especially, the signals of the protons of the phosphonium moieties, expected to be involved in hydrogen bond formation, were not shifted.

With ligand **6** as with **5**, only one singlet for the phosphorus atoms was detected in its ^{31}P NMR spectrum, indicating all the four phosphonium groups being chemically equivalent. In the presence of sodium perchlorate and thiocyanate, the changes in chemical shifts are larger than those observed with the disubstituted derivatives and suggest stronger interactions (Table 1). With all ligands, the most important values were observed for perchlorate.

^{1}H NMR studies in acetonitrile

^{1}H NMR experiments were repeated with **5** and sodium perchlorate in deuterated acetonitrile, a more dissociating solvent, in which association phenomena are not as important as in chloroform (*22*). The spectra of the ligand are very similar in both the solvents. In acetonitrile, the addition of $NaClO_4$ induces shifts of the same signals as in chloroform. Moreover, this study showed the influence of the counterion of the salts on the shifts observed in the spectra (see Table S4, Supplementary Material). The signal of the methylene protons (g) adjacent to the phenolic oxygen atoms was shifted only with $NaClO_4$ and $LiClO_4$. With both salts, the shifts corresponding to the signals of the protons (j) next to the phosphorus atoms (which are supposed to interact with perchlorate) were similar, whereas with Et_4NClO_4 and especially with $CsClO_4$, the values were very small. The changes observed suggested that the ligand–anion interaction was connected with the nature of the counterion and its affinity for the ligand.

In order to observe the influence of the ligand counterion, bromide anions were replaced by the more lipophilic perchlorate (**5a** and **6a**) or hexafluorophosphate (**5b** and **6b**) anions. The chemical shifts (δ) of selected protons, given in Table 2, show only slight differences for protons (c,e,f) and (g) close to the calix[4]arene scaffold ($\Delta\delta$ in the range 0.02–0.07 ppm). In contrast, the signals of the protons (j) next to the charged phosphorus atoms are

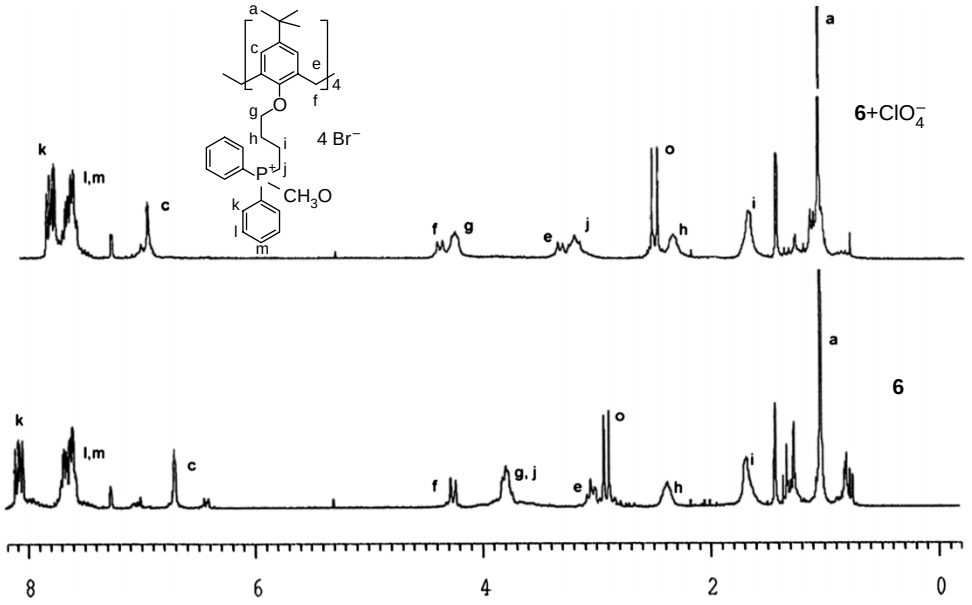


Figure 3. ^{1}H NMR spectra of ligand **6** alone and in the presence of ClO_4^- in $CDCl_3$.

Table 2. Differences ($\Delta\delta$) in the proton chemical shifts (δ) (ppm) in the spectra of ligands **5** and **6**, **5a** and **6a**, **5b** and **6b** in CD_3CN.

	c	e	f	g	j	o
δ (**5**)	6.87	2.93	4.15	3.74	3.81	–
δ (**5a**)	6.83	2.91	4.11	3.76	3.17	–
$\Delta\delta$ (**5a**–**5**)	−0.04	−0.02	−0.04	0.02	−0.64	–
δ (**5b**)	6.80	2.87	4.09	3.77	3.06	–
$\Delta\delta$ (**5b**–**5**)	−0.07	−0.06	−0.06	0.03	−0.75	–
δ (**6**)	6.92	3.02	4.19	3.70	3.58	2.78
δ (**6a**)	6.89	2.98	4.15	3.73	2.85	2.37
$\Delta\delta$ (**6a**–**6**)	−0.03	−0.04	−0.04	0.03	−0.73	−0.41
δ (**6b**)	6.88	2.97	4.12	3.75	2.75	2.32
$\Delta\delta$ (**6b**–**6**)	−0.04	−0.05	−0.07	0.05	−0.83	−0.46

greatly shifted ($\Delta\delta = -0.64$ ppm for **5a**, -0.75 ppm for **5b** and $\Delta\delta = -0.73$ ppm for **6a**, -0.83 ppm for **6b**). With ligands **6a** and **6b**, the signals of the protons (o) of the methyl substituents are also displaced ($\Delta\delta = -0.41$ ppm for **6a** and -0.46 ppm for **6b**). These results show that the chemical shifts of the protons next to the phosphonium groups are influenced by the ligand counterion.

On the other hand, it was also shown that when the lipophilic PF_6^- anions were replacing the Br^- counterions of the ligand, there was still a significant shift of the protons (j) close to the phosphorus atoms for ligand **5b** in the presence of ClO_4^- (Table S4) (*22*). This result suggested complexation of perchlorate with this ligand, where no exchange is normally possible.

Microcalorimetric studies in acetonitrile

In order to get more information on the influence of the counterion of the salt, microcalorimetric titrations were carried out with ligands **5** and **5b** against $NaClO_4$, $LiClO_4$ and Et_4NClO_4 in acetonitrile. The thermograms recorded during the titration of these ligands with $NaClO_4$ and $LiClO_4$ showed significant exothermic heat effects, whereas their titration with Et_4NClO_4 led to no thermal effect (see Figure S1, Supplementary Material). For comparison purpose, the titration of monomer **8** with $NaClO_4$ was also carried out showing no significant heat effect.

If only the ClO_4^- anion were involved in the complexation, a similar heat effect should be observed in all the titrations. The fact that an effect is only observed for $NaClO_4$ and $LiClO_4$ suggests that it is not only related to the anion interaction (complexation or anion exchange). Assuming that the large tetraethylammonium cation cannot be complexed with a calix[4]arene, the heat effects observed during the titration with $NaClO_4$ and $LiClO_4$ would rather be due to the complexation of the cations with the two ligands. This is supported by the fact that no heat effect was detected with monomer **8**, supposed to be unable to complex these cations.

Calorimetric data obtained with $NaClO_4$ and $LiClO_4$ were interpreted assuming different cation complexation models. With sodium and both ligands, the best fit was obtained by considering the presence of ML and ML_2 complexes. The same species were found with $LiClO_4$ and **5b**, whereas only a 1:1 complex was formed with **5**. The formation of ML_2 species could be explained by the complexation of the ion pair $Na^+ClO_4^-$ by two ligands. The stability constants of these complexes are given in Table S5 (see the Supplementary Material).

An important heat effect was observed during the titration of ligands **5** and **5b** against LiBr, which should be related directly to cation complexation as no anion exchange is possible with these ligands. The data interpretation led to species of the same stoichiometry as with $LiClO_4$ (Table S5). The values of the stability constants of 1:1 species formed in the presence of $LiClO_4$ and LiBr are comparable (with **5**, $\log\beta = 3.24$ and 3.15, respectively, and with **5b**, $\log\beta = 4.29$ and 4.32, respectively). They are lower than that of the complex formed by the tetra-methylated *p-tert*-butylcalix[4]arene with lithium ($\log\beta = 5.10$ in acetonitrile (*28*)).

All that considered, the UV spectrophotometric titrations of ligand **5** against ClO_4^- previously performed may certainly be interpreted in terms of cation rather than anion complexation (*22*). The values of the stability constants of the 1:1 complexes with sodium perchlorate ($\log\beta = 3.81 \pm 0.02$) and with lithium perchlorate ($\log\beta = 3.71 \pm 0.04$) (*22*) are of the same order of magnitude as those obtained from microcalorimetric measurements.

Potentiometric studies

Only few ligands containing phosphorus atoms have been studied so far as active material in ion-selective membrane electrodes (*29–31*). They showed a selective response for ClO_4^-, with, however, little discrimination with respect to I^- and SCN^-. The results suggested a particular affinity of ligands containing phosphorus atoms for ClO_4^-, SCN^- and I^- anions. By attaching phosphonium moieties to a calix[4]arene scaffold and taking advantage of the preorganisation of the ligand, it was expected to enhance

the selectivity for tetrahedral or spherical anions. Such selectivity (especially for ClO_4^- over I^-) is hard to obtain with other kinds of receptors.

Disubstituted phosphonium ligands **1** and **2** were tested as ionophores in the membrane electrodes. The electrodes were sensitive to perchlorate, thiocyanate, iodide and nitrate, showing fast, near-Nernstian responses (Figure 4 and Table S6 of the Supplementary Material). However, their characteristics changed with time. Attempts to optimise the composition of the conditioning solutions as well as the conditioning time did not improve the situation, which might be due to slow leakage of the ionophores from the membrane. These ligands had also the tendency to crystallise in the membrane phase. Crystallisation of our ligands within the membranes depends strongly on the kind of plasticiser used. The ligands in the membranes based on bis-(2-ethylhexyl)sebacate (BEHS) crystallised strongly, which decreased their stability. This phenomenon originates from the higher lipophilicity of this plasticiser ($\log P = 10.1$) as compared to 2-nitrophenyloctylether (*o*-NPOE) ($\log P = 5.9$) (*32*), which is more suitable for charged ligands. Electrodes with membranes based on *o*-NPOE had the best lifetime and response characteristics and were chosen for further studies.

The more lipophilic ligands **3** and **4**, in which *n*-propyl chains replace the two phenolic OH groups, were also synthesised. The lifetime of electrodes incorporating these ligands for perchlorate was increased to at least 3 weeks. The repeatability of the measurements was also good, but their detection limits increased (see Table S7, Supplementary Material).

The membranes of electrodes incorporating the tetra-substituted ligand **6** showed rather quick (within 15–20 s), stable and fully reversible responses (Figure 5 and Table S8 of the Supplementary Material). The repeatability of the measurements was also good and their lifetime was more than 3 weeks. They showed close to Nernstian response for ClO_4^-, I^-, NO_3^- and SCN^- and no significant response for SO_4^{2-}, CO_3^{2-}, HPO_4^{2-}, PO_4^{3-}. A similar behaviour was already observed for electrodes incorporating ligand **5** (Table S8). The highest selectivity was obtained for ClO_4^- ions in buffered solution (pH 5.5) and in water (pH 6.5). The over-Nernstian slope of the electrode response for $Cr_2O_7^{2-}$ could indicate a mechanism where both processes, anion complexation and anion exchange, play an important role. It can also be explained as the presence of different forms of chromate in the sample.

While the addition of lipophilic anionic sites (KTClPB) to the membranes in the case of ligand **5** did not change much the properties of the electrodes, it affected the properties of the electrodes containing **6** (Table 3). Without the salt, the slope of the electrode is -54.2 mV, and slightly decreases to -51.8 and -49.9 mV, respectively, in the presence of the salt. According to the literature data (*29*, *31*), such results suggest that none of the ligands works as a neutral carrier because the addition of the lipophilic anion to the membrane does not induce a cationic response of the potentiometric cell. Ligand **6** seems to work in the membrane as a typical anion exchanger, whereas ligand **5** could be considered as a charged ligand despite the small influence of KTClPB.

The influence of the ligand counterions (Br^-, ClO_4^-, PF_6^-) on the properties of the membrane electrodes was also studied. Table 4 compares the responses of perchlorate of electrodes based on ligands **5a** and **6a** (perchlorates) and on ligands **5b** and **6b** (hexafluorophosphates) to the corresponding electrodes based on ligands **5** and **6** (bromides). The less good slope of the electrodes containing **6a** and **6b** as compared to that of the electrodes containing **6** suggests rather the anion exchange nature of the latter ligand. In this case, the presence of more lipophilic anions (perchlorate or hexafluorophosphate)

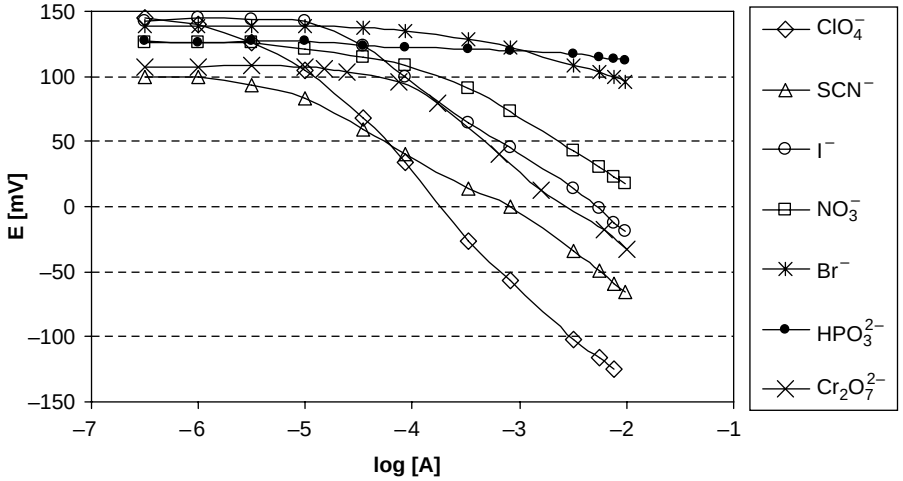


Figure 4. Potentiometric anion responses of electrodes with the PVC/NPOE membrane containing ligand **1** in MES buffer at pH 5.5.

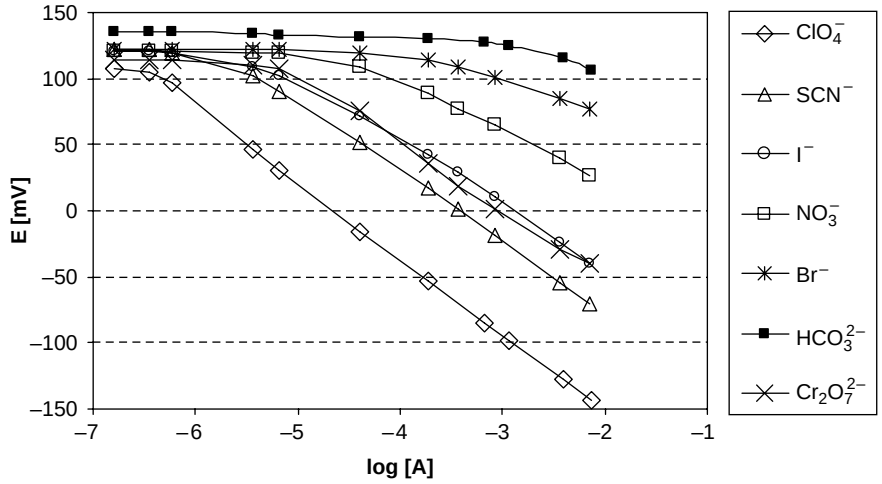


Figure 5. Potentiometric anion responses of electrodes with the PVC/NPOE membrane containing ligand **6** in MES buffer at pH 5.5.

slows down the anion exchange process. In contrast, the properties of electrodes with the bromide ligand **5** and with the perchlorate ligand **5a** are comparable. The presence of highly lipophilic perchlorate anions does not disturb the electrode response, while the presence of hexafluorophosphate anions in the membrane phase (electrode containing ligand **5b**) decreases the slope and the linearity range.

The poorer properties of the electrode containing **5b** and **6b** could be explained by the higher lipophilicity of hexafluorophosphate anions which hinders the process of anion exchange. The complexation of ClO_4^- by ligand **5** could explain the good response of electrodes based on **5** and **5a** to perchlorate. Such interpretation is consistent with the results of previous experiments (Table 4) and indicates that ligand **5** behaves more like a charged carrier for ClO_4^-, while ligand **6** behaves more as an anion exchanger.

The order of selectivity observed for all phosphonium ligands **1**–**6** and **8** follows the Hofmeister series:

$$ClO_4^- > SCN^- > I^- > Cr_2O_7^{2-} > NO_3^- > Br^- > HCO_3^- > HPO_4^{2-} > SO_4^{2-}.$$

The highest selectivity is observed for perchlorate (Table 5).

The electrodes based on tetraphosphonium derivatives show higher selectivities for perchlorate over thiocyanate, iodide and nitrate than those based on their diphosphonium counterparts. These selectivities are also better than the selectivity of electrodes based on monomer **8**.

The replacement of one phenyl substituent on the phosphorus atoms by one methyl group does not change significantly the selectivity pattern and the values of the selectivity coefficients of the electrodes containing either di- or tetraphosphonium ligands. The only exception is the selectivity of the electrodes based on compound **5** against $Cr_2O_7^{2-}$, which increases from 2.6 to 3.2 log units.

Electrodes based on alkylated compounds **3** and **4** are also selective for perchlorate but the selectivity over iodide and thiocyanate is decreased (Table 5).

Ligands **5** and **6** display better potentiometric properties than the protonated cyclam (*33*) or its copper complex (*34*) than a phosphodithiamacrocycle (*35*). For instance, the detection limit is 2.5×10^{-7} M with ligand **5** when compared to 4.2×10^{-6} M for the cyclam and 8×10^{-7} M for the phosphodithiamacrocycle. Ligand **6** as **5** presents generally higher selectivities than TDMACl (*36*), the protonated cyclam and $[Cu(cyclam)]^{2+}$.

Table 3. Characteristics of potentiometric responses for perchlorate of PVC/NPOE electrodes containing ligands **5** and **6** and different amounts of KTClPB.

Ligand	KTClPB (mol%)	*S* (mV/decade)	LR (log[A])
5	0	−55.6	−6.0
5	40	−54.6	−6.0
5	120	−55.9	−5.7
6	0	−54.2	−6.0
6	40	−51.8	−6.0
6	120	−49.9	−5.7

Notes: Inner and conditioning electrolyte, MES/NaOH, pH = 5.5/10^{-2} M NaCl.

Table 4. Characteristics of potentiometric responses for perchlorate of PVC/NPOE electrodes containing tetra-substituted phosphonium ligands with different counterions.

Ligand	Counterion	*S* (mV/decade)	LR (log[A])
5	Br^-	−56.5	−6.0
5a	ClO_4^-	−56.1	−6.0
5b	PF_6^-	−38.3	−5.5
6	Br^-	−54.4	−5.7
6a	ClO_4^-	−40.4	−6.0
6b	PF_6^-	−36.2	−6.0

Notes: Inner and conditioning electrolyte, MES/NaOH, pH = 5.5/10^{-2} M NaCl.

Table 5. Selectivity coefficients as $\log K^{pot}_{ClO_4^-,X}$ of the PVC/NPOE membrane electrodes based on phosphonium calixarenes **1**–**6** and monomer **8**.

	$\log K^{pot}_{ClO_4^-,X}$						
Anion X	**1**	**2**	**3**	**4**	**5**	**6**	**8**
ClO_4^-	0	0	0	0	0	0	0
SCN^-	−1.2	−1.4	−1.1	−0.6	−1.3	−1.4	−1.1
I^-	−1.7	−1.7	−1.3	−0.9	−2.0	−2.0	−1.6
NO_3^-	−2.6	−2.6	−2.4	−1.9	−2.9	−3.0	−2.5
HCO_3^-	−4.6	−4.5	−4.6	−4.4	−4.6	−4.4	ND
$Cr_2O_7^{2-}$	−2.2	−2.4	−2.6	−1.7	−2.6	−3.2	−1.9
HPO_4^{2-}	−4.5	−4.5	−4.5	−4.4	−4.5	−4.4	ND
SO_4^{2-}	−4.9	−4.7	−4.7	−4.7	−4.7	−4.5	ND

Note: ND, not determined.

Concluding remarks

The different techniques used to assess the binding properties of phosphonium derivatives showed strong interactions with SCN^-, I^- and especially with ClO_4^-, and pointed out the important role played by the salt counterion (Na^+ or Li^+), which may be complexed by the calix[4]arene. Incorporated in the PVC membrane electrodes, these molecules are efficient sensing material for anions with a selectivity order following the Hofmeister series generally observed for ion exchangers. However, the electrodes based on tetraphosphonium derivatives showed better selectivities than those based on the diphosphonium analogues or on the monomeric unit, indicating the importance of the ligand preorganisation which cannot be observed in the case of simple anion exchangers.

A question which must be addressed concerns the nature of the interaction between the ligands and the anions, e.g. ClO_4^-. Is it a simple ion exchange between the bromides of the ligand and this more lipophilic anion, or is it complexation within the charged phosphonium groups? What is the exact role of the salt counterion?

If NMR gives some indications on the changes in the molecule, suggesting interactions, it does not tell if there is complexation or anion exchange, since the nature of the counterion of the ligand has been shown to influence the chemical shifts of the protons near the charged atoms. In favour of ion exchange is the fact that the most important shifts are observed with the more lipophilic anions ClO_4^-, SCN^- and I^-. The behaviour of selective electrodes is also consistent with this assumption. However, the fact that no change occurred in the spectrum of the monomer, where only exchange is possible, is against this hypothesis. In favour of complexation is the fact that, in the presence of $NaClO_4$, strong shifts are observed for the signals of the protons next to the phosphonium groups in the spectrum of the hexafluorophosphate ligand where no exchange is possible.

On the other hand, ^{1}H NMR and microcalorimetry emphasised the importance of the cation, which can be complexed in the cavity of the calixarene. With perchlorate, the best interaction takes place with Na^+ and Li^+, whereas little or no interaction occurs with the larger Et_4N^+ and Cs^+. It can also be noted that the anion also plays a role in the complexation of the cation, since the spectrum of the calixarene part is not affected in the presence of NO_3^-, SO_4^{2-}, HCO_3^- and $Cr_2O_7^{2-}$, i.e. the less lipophilic ones.

Experimental

FAB mass spectra were obtained on a VG analytical ZAB HF instrument. All reagents and solvents were commercial and used without further purification.

Chromatography columns were prepared from Kieselgel Merck Si 60 (40–63 μm). TLC was performed on 250 μm silica gel plates (Merck, Darmstadt, Germany) containing a fluorescent indicator.

Synthesis of intermediate compounds

*1,3-Bis-(butoxy-4-bromide)-p-tert-butylcalix[4]arene (**S₂**)*

Into a 250 cm^3 flask containing tetrakis-*p-tert*-butylcalix[4]arene **S₁** (3.244 g, 5.00 mmol) and acetone (50 cm^3), K_2CO_3 (1.383 g, 10.00 mmol) was added. The mixture was stirred at room temperature for 2 h. Then, 1,4-butyldibromide (3.236 g, 15.00 mmol) in acetone (50 cm^3) was added. The mixture was left for 4 days under reflux. After 4 days, methanol (5 cm^3) was added. The solvents were evaporated, and the reaction mixture was dissolved in dichloromethane (100 cm^3). After extraction with water (150 cm^3), the organic phase was dried with Na_2SO_4 and evaporated. The crude product was purified by crystallisation from a 1:10 dichloromethane–methanol mixture giving compound **S₂** (3.252 g, 3.54 mmol) in 71% yield. Mp > 280°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.98 (s, 18H, C—(CH_3)$_3$), 1.30 (s, 18H, C—(CH_3)$_3$), 2.15 (qn, 4H, J = 4.4 Hz, CH_2—CH_2—O), 2.32 (qn, 4H, J = 4.2 Hz, CH_2—CH_2—Br), 3.32 (d, 4H, J = 13.0 Hz, Ar-CH_2-Ar), 3.65 (t, 4H, J = 6.6 Hz, CH_2—CH_2—Br), 4.01 (t, 4H,

$J = 5.8$ Hz, CH_2—CH_2—O), 4.25 (d, 4H, $J = 13.0$ Hz, Ar-CH_2-Ar), 6.78 (s, 4H, Ar-*H*), 7.08 (s, 4H, Ar-*H*), 7.40 (s, 2H, *OH*). Anal. Calcd for $C_{52}H_{70}O_4Br_2$: C, 67.97; H, 7.68. Found: C, 68.21; H, 7.94.

*1,3-Bis-(propoxy)-p-tert-butylcalix[4]arene (**S$_3$**)*

Into a 250 cm^3 flask containing tetrakis-*p-tert*-butylcalix[4]arene **S$_1$** (3.244 g, 5.00 mmol) and acetone (50 cm^3), K_2CO_3 (1.383 g, 10.00 mmol) was added. The mixture was stirred at room temperature for 2 h. Then, bromopropane (1.845 g, 15.00 mmol) in acetone (40 cm^3) was added. The mixture was left for 4 days under reflux. After 4 days, methanol (5 cm^3) was added. The solvents were evaporated, and the reaction mixture was dissolved in dichloromethane (100 cm^3). After extraction with water (150 cm^3), the organic phase was dried with Na_2SO_4 and evaporated. The crude product was purified by crystallisation from a 1:9 acetone–methanol mixture giving the pure compound **S$_3$** (2.016 g, 2.75 mmol) in 55% yield. Mp > 280°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 1.02 (s, 18H, C—(CH_3)$_3$), 1.27 (t, 6H, $J = 5.0$ Hz, CH_3—CH_2—), 1.28 (s, 18H, C—(CH_3)$_3$), 2.06 (sx, 4H, $J = 4.9$ Hz, CH_3—CH_2—CH_2—O), 3.32 (d, 4H, $J = 12.8$ Hz, Ar-CH_2-Ar), 3.96 (t, 4H, $J = 5.9$ Hz, O—CH_2—CH_2), 4.31 (d, 4H, $J = 12.8$ Hz, Ar-CH_2-Ar), 6.86 (s, 4H, Ar-*H*), 7.05 (s, 4H, Ar-*H*), 7.89 (s, 2H, *OH*). Anal. Calcd for $C_{50}H_{68}O_4$: C, 81.92; H, 9.35. Found: C, 82.05; H, 9.40.

*1,3-Bis-(propoxy)-2,4-bis-(butoxy-4-bromide)-tetrakis-p-tert-butylcalix[4]arene (**S$_4$**)*

Into a 250 cm^3 flask containing **S$_3$** (2.016 g, 2.75 mmol) and DMF (50 cm^3), NaH (0.480 g, 20.00 mmol) was added. NaH was washed twice with hexane before addition. The mixture was stirred at room temperature for 4 h. After this time, 1,4-dibromobutyl (5.940 g, 27.5 mmol) in DMF (40 cm^3) was added. The mixture was left for 2 days at 80–90°C. After 2 days, methanol (30 cm^3) was added. The solvents were evaporated and the reaction mixture was dissolved in dichloromethane (100 cm^3). After extraction with water (250 cm^3), the organic phase was dried with Na_2SO_4 and evaporated. The crude product was purified by crystallisation from a 1:10 dichloromethane–methanol mixture giving compound **S$_4$** (1.584 g, 1.57 mmol) in 57% yield. Mp 170°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 1.01 (t, 6H, $J = 5.2$ Hz, CH_3—CH_2—), 1.05 (s, 18H, C—(CH_3)$_3$), 1.12 (s, 18H, C—(CH_3)$_3$), 1.99–2.05 (m, 4H, CH_3—CH_2—), 2.07–2.25 (m, 8H, —CH_2—CH_2—CH_2—Br), 3.13 (d, 4H, $J = 13.0$ Hz, Ar-CH_2-Ar), 3.51 (t, 4H, $J = 6.6$ Hz, —CH_2—Br), 3.81 (t, 4H, $J = 5.8$ Hz, CH_3—CH_2—CH_2—O), 3.91 (t, 4H, $J = 5.8$ Hz, Br—CH_2—CH_2—CH_2—CH_2—O), 4.39 (d, 4H, $J = 13.0$ Hz, Ar-CH_2-Ar), 6.74 (s, 4H, Ar-*H*), 6.83 (s, 4H, Ar-*H*). Anal. Calcd for $C_{58}H_{82}O_4Br_2$: C, 69.45; H, 8.24. Found: C, 69.65; H, 8.30.

*Tetrakis-(butoxy-4-bromide)-tetrakis-p-tert-butylcalix[4]arene (**S$_5$**)*

The suspension of *p-tert*-butylcalix[4]arene **S$_1$** (1.947 g, 3.00 mmol) and NaH in oil washed three times with hexane (0.700 g, 29.17 mmol) was stirred at room temperature in DMF (50 cm^3) for 1 h. Then, 1,4-dibromobutane (12.947 g, 59.06 mmol) was added and the mixture was heated to 80°C. After 4 days of heating, the mixture was cooled and MeOH (20 cm^3) was added. After removal of the solvent, the residue was dissolved in dichloromethane and water and acidified with 1 M HCl. The organic layer was dried over Na_2SO_4, filtered and evaporated. After precipitation from methanol, the pure compound **S$_5$** (1.520 g, 1.28 mmol) was obtained in 43% yield. Mp 180°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.09 (s, 36H, —C(CH_3)$_3$), 1.98–2.09 (m, 8H, —CH_2—), 2.16–2.23 (m, 8H, —CH_2—), 3.15 (d, 4H, $J = 13.0$ Hz, Ar-CH_2-Ar), 3.53 (t, 8H, $J = 6.9$ Hz, —CH_2—Br), 3.91 (t, 8H, $J = 6.9$ Hz, —CH_2—O—), 4.36 (d, 4H, $J = 13.0$ Hz, Ar-CH_2-Ar), 6.79 (s, 8H, Ar-*H*). Anal. Calcd for $C_{60}H_{84}O_4Br_4$: C, 60.61; H, 7.12; Found: C, 60.87; H, 7.32.

*Tetrakis-(4-(diphenylphosphine)-butoxy)-p-tert-butylcalix[4]arene (**S$_6$**)*

Into a 100 cm^3 flask containing compound **S$_5$** (1.510 g, 1.27 mmol) of freshly distilled THF (10 cm^3), $KP(Ph)_2$ (1.282 g, 5.72 mmol) in THF (15 cm^3) was added via a syringe. The mixture was stirred for 2 h at room temperature, during which the colour of the reaction mixture changed from red to dark yellow. The mixture was then evaporated and extracted twice with dichloromethane (30 cm^3). Purification of the crude product on silica column with a 3:7 dichloromethane–hexane mixture as the eluent gave compound **S$_6$** (0.409 g, 0.26 mmol) in 20% yield. Mp 110°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.08 (s, 36H, —C(CH_3)$_3$), 1.42–1.63 (m, 8H, —CH_2—CH_2—P), 2.00–2.18 (m, 8H, —CH_2—CH_2—O), 2.00–2.18 (m, 8H, —CH_2—P), 3.05 (d, 4H, $J = 12.9$ Hz, Ar-CH_2-Ar), 3.81 (t, 8H, $J = 5.4$ Hz, —CH_2—CH_2—O), 4.29 (d, 4H, $J = 12.9$ Hz, Ar-CH_2-Ar), 6.75 (s, 8H, Ar-*H*), 7.20–7.46 (m, 40H, P-Ar-*H*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): −14.91 [P]. *m/z* (MALDI) 1610.88 $(M+H)^+$. Anal. Calcd for $C_{108}H_{124}O_4P_4$: C, 80.57; H, 7.76; Found: C, 80.73; H, 7.87.

Synthesis of phosphonium ligands

*1,3-Bis-(4-triphenylphosphonium-butoxy)-p-tert-butylcalix[4]arene dibromide (**1**)*

Into a 100 cm^3 flask containing **S$_2$** (1.184 g, 2.00 mmol) in chloroform (30 cm^3), triphenylphosphine (5.248 g, 20.00 mmol) in chloroform (20 cm^3) was added. After 6 days under reflux, the mixture was cooled and the solvent

was evaporated. The residue was dissolved in dichloromethane. The excess of triphenylphosphine was precipitated from methanol and filtered out. The filtrate was evaporated. The pure product **1** (2.179 g, 1.51 mmol) was obtained by precipitation from a 1:9 dichloromethane–hexane mixture, as a white–light green powder in 76% yield: Mp > 280°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.99 (s, 18H, —C(C*H*$_3$)$_3$), 1.28 (s, 18H, —C(C*H*$_3$)$_3$), 2.05–2.29 (m, 8H, CH_2—*CH*$_2$—*CH*$_2$—CH_2—O), 3.19 (d, 4H, J = 12.8 Hz, Ar-*CH*$_2$-Ar), 3.80–4.00 (m, 4H, —*CH*$_2$—O), 3.90 (d, 4H, J = 12.8 Hz, Ar-*CH*$_2$-Ar), 3.90–4.08 (m, 4H, —*CH*$_2$—P), 6.79 (s, 4H, Ar-*H*), 6.99 (s, 4H, Ar-*H*), 7.49 (s, 2H, *OH*), 7.54–7.64 (m, 12H, P-Ar-*H meta*), 7.65–7.74 (m, 6H, P-Ar-*H para*), 7.80–7.93 (m, 12H, P-Ar-*H ortho*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 25.80. *m/z* (FAB$^+$) 721.7 (M+2H)$^{2+}$; *m/z* (MALDI) 1361.7 (M−Br)$^+$. Anal. Calcd for $C_{88}H_{100}O_4P_2Br_2$: C, 73.22; H, 6.98. Found: C, 73.46; H, 7.20.

*1,3-Bis-(4-(P,P-diphenyl-P-methylphosphonium)-butoxy)-p-tert-butylcalix[4]arene dibromide (**2**)*

Compound **2** was prepared following the same procedure as for compound **1** with **S$_2$** (2.753 g, 3.00 mmol) and diphenylmethylphosphine (6.006 g, 30.00 mmol) in 69% yield. Mp > 280°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.96 (s, 18H, —C(*CH*$_3$)$_3$), 1.29 (s, 18H, —C(*CH*$_3$)$_3$), 1.91–2.10 (m, 4H, —*CH*$_2$—CH_2—P), 2.11–2.27 (m, 4H, —*CH*$_2$—CH_2—O), 2.99 (d, 6H, J = 13.8 Hz, *CH*$_3$—P), 3.23 (d, 4H, J = 13.5 Hz, Ar-*CH*$_2$-Ar), 3.58–3.75 (m, 4H, —*CH*$_2$—P), 3.90 (t, 4H, J = 5.3 Hz, —*CH*$_2$—O), 4.02 (d, 4H, J = 13.5 Hz, Ar-*CH*$_2$-Ar), 6.76 (s, 4H, Ar-*H*), 7.01 (s, 4H, Ar-*H*), 7.31 (s, 2H, *OH*), 7.48–7.59 (m, 8 H, P-Ar-*H meta*), 7.61–7.70 (m, 4H, P-Ar-*H para*), 7.90–8.06 (m, 8H, P-Ar-*H ortho*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 25.96. *m/z* (MALDI) 1239.58 (M−Br)$^+$. Anal. Calcd for $C_{78}H_{96}O_4P_2Br_2$: C, 71.01; H, 7.33. Found: C, 71.21; H, 7.52.

*1,3-Bis-(4-triphenylphosphonium-butoxy)-2,4-bis-propoxy-p-tert-butyl-calix[4]arene dibromide (**3**)*

Into a 100 cm^3 flask containing **S$_4$** (2.012 g, 2.00 mmol) in chloroform (30 cm^3), triphenylphosphine (5.248 g, 20.00 mmol) in chloroform (20 cm^3) was added and left for 6 days under reflux. After that time, the mixture was cooled and the solvent was evaporated. The residue was dissolved in dichloromethane. The excess of triphenylphosphine was precipitated from methanol and filtered off. The filtrate was evaporated. The pure product **3** (2.179 g, 1.51 mmol) was obtained by precipitation from a 1:9 dichloromethane–hexane mixture, as a white–light green powder in 76% yield. Mp 120°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.86 (t, 6H, J = 5.3 Hz, *CH*$_3$—CH_2—CH_2—O), 0.99 (s, 18H, —C(C*H*$_3$)$_3$), 1.11 (s, 18H, —C(C*H*$_3$)$_3$), 1.65–1.87 (m, 4H, CH_3—*CH*$_2$—CH_2—O), 1.77–1.94 (m, 4H, —*CH*$_2$—CH_2—P), 2.28–2.43 (m, 4H, —*CH*$_2$—CH_2—O), 2.95 (d, 4H, J = 13.0 Hz, Ar-*CH*$_2$-Ar), 3.63 (t, 4H, J = 5.9 Hz, CH_3—CH_2—*CH*$_2$—O), 3.85–4.00 (m, 4H, —*CH*$_2$—P), 3.85–4.00 (m, 4H, —*CH*$_2$—O), 4.18 (d, 4H, J = 13.0 Hz, Ar-*CH*$_2$-Ar), 6.61 (s, 4H, Ar-*H*), 6.76 (s, 4H, Ar-*H*), 7.60–7.92 (m, 30H, P-Ar-*H ortho, meta, para*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 25.84. *m/z* (MALDI) 1447.6 (M−Br)$^+$. Anal. Calcd for $C_{94}H_{112}O_4P_2Br_2$: C, 73.91; H, 7.39. Found: C, 73.67; H, 7.66.

*1,3-Bis-propoxy-2,4-bis-(4-(P,P-diphenyl-P-methylphosphonium)-butoxy)-p-tert-butylcalix[4]arene dibromide (**4**)*

Compound **4** was obtained according to the same procedure as for **3** with **S$_4$** (3.050 g, 3.04 mmol) and diphenylmethylphosphine (6.006 g, 30.00 mmol) as a white powder in 64% yield. Mp 148°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.79 (s, 18H, —C(*CH*$_3$)$_3$), 1.03 (t, 6H, J = 6.9 Hz, *CH*$_3$—CH_2—CH_2—O), 1.31 (s, 18H, —C(*CH*$_3$)$_3$), 1.55–1.75 (m, 4H, —*CH*$_2$—CH_2—P), 1.88–2.04 (m, 4H, CH_3—*CH*$_2$—CH_2—O), 2.40–2.58 (m, 4H, CH_2—*CH*$_2$—CH_2—O), 3.05 (d, 4H, J = 12.5 Hz, Ar-*CH*$_2$-Ar), 3.23 (d, 6H, J = 14.3 Hz, *CH*$_3$—P), 3.62–3.80 (m, 8H, —*CH*$_2$—P and —*CH*$_2$—O), 3.88 (t, 4H, J = 5.9 Hz, —CH_2—CH_2—*CH*$_2$—O), 4.32 (d, 4H, J = 12.5 Hz, Ar-*CH*$_2$-Ar), 6.43 (s, 4H, Ar-*H*), 7.08 (s, 4H, Ar-*H*), 7.60–7.80 (m, 12H, P-Ar-*H meta, para*), 8.01–8.13 (m, 8H, P-Ar-*H ortho*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 25.98. *m/z* (MALDI) 1323.7 (M−Br)$^+$. Anal. Calcd for $C_{84}H_{108}O_4P_2Br_2$: C, 71.88; H, 7.76. Found: C, 71.99; H, 7.85.

*Tetrakis-(4-triphenylphosphonium-butoxy)-tetrakis-p-tert-butylcalix[4]arene tetrabromide (**5**)*

Compound **S$_5$** (1.184 g, 1.00 mmol) was dissolved in chloroform (30 cm^3). After a few minutes of stirring, triphenylphosphine (5.248 g, 20.00 mmol) and chloroform (20 cm^3) were added. After 6 days of refluxing, the mixture was cooled and the solvent was evaporated. The residue was dissolved in dichloromethane. The excess of triphenylphosphine was precipitated from methanol and filtered. The organic layer was evaporated. Chromatography on a silica column with a 90:10 dichloromethane–methanol mixture as the eluent gave compound **5** (0.67 g, 0.30 mmol) in 30% yield. Mp 132°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.02 (s, 36H, —C(C*H*$_3$)$_3$), 1.56–1.72 (m, 8H, —C*H*$_2$—), 2.24–2.41 (m, 8H, —C*H*$_2$—), 2.91 (d, 4H, J = 13.0 Hz, Ar-C*H*$_2$-Ar), 3.78–4.01 (m, 16H, —C*H*$_2$—P and Ar-O—C*H*$_2$), 4.23 (d, 4H, J = 13.0 Hz, Ar-C*H*$_2$-Ar), 6.63 (s, 8H, Ar-*H*), 7.59–7.71 (m, 36H, P-Ar-*H*, *meta, para*), 7.76–7.88 (m, 24H, P-Ar-*H, ortho*). ^{31}P NMR

(400 MHz, $CDCl_3$) δ (ppm): 25.76. *m/z* (FAB^+) 479.5 $(M)^{4+}$; *m/z* (MALDI) 2157.7 $(M-Br)^+$. Anal. Calcd for $C_{132}H_{144}O_4P_4Br_4$: C, 70.84; H, 6.49. Found: C, 70.97; H, 6.69.

*Tetrakis-(4-triphenylphosphonium-butoxy)-p-tert-butylcalix[4]arene tetraperchlorate (**5a**)*

Into a 10 cm^3 flask, **5** (0.100 g, 0.045 mmol) was dissolved in acetonitrile (1 cm^3). $AgClO_4$ (0.050 g, 0.241 mmol) in acetonitrile (1 cm^3) was added dropwise to the ligand solution. After 24 h of stirring at room temperature, the precipitate of AgBr was filtered off. The filtrate was evaporated to give compound **5a** (0.088 g, 0.038 mmol) in 84% yield. Mp > 120°C decomposition. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.07 (s, 36H, —C(*CH*$_3$)$_3$), 1.70–1.85 (m, 8H, —*CH*$_2$—CH$_2$—P), 2.45–2.53 (m, 8H, —*CH*$_2$—CH$_2$—O), 2.95 (d, 4H, *J* = 13.0 Hz, Ar-*CH*$_2$-Ar), 3.43–3.60 (m, 8H, —*CH*$_2$—P), 4.20–4.30 (m, 8H, —*CH*$_2$—O), 4.44 (d, 4H, *J* = 13.0 Hz, Ar-*CH*$_2$-Ar), 6.97 (s, 8H, Ar-*H*), 7.56–7.90 (m, 60H, P-Ar-*H*, *ortho, meta, para*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 24.54. *m/z* (MALDI) 2214.2 $(M-ClO_4)^+$. Anal. Calcd for $C_{132}H_{144}O_4P_4(ClO_4)_4$: C, 68.45; H, 6.27. Found: C, 68.70; H, 6.45.

*Tetrakis-(4-triphenylphosphonium-butoxy)-tetrakis-p-tert-butylcalix[4]arene tetrahexafluorophosphate (**5b**)*

Compound **5** (0.100 g, 0.045 mmol) was dissolved in acetonitrile (1 cm^3). Then, $AgPF_6$ (0.062 g, 0.245 mmol) was dissolved in acetonitrile and added dropwise to the ligand solution. After 24 h, the precipitate of NaBr was removed and the solution was evaporated. Compound **5b** (0.090 g, 0.036 mmol) was obtained in 80% yield. Mp 128°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 1.12 (s, 36H, —C(C*H*$_3$)$_3$), 1.65–1.81 (m, 8H, —C*H*$_2$—), 2.38–2.49 (m, 8H, —C*H*$_2$—), 3.25–3.38 (m, 8H, —C*H*$_2$—P), 3.47 (d, 4H, *J* = 13.0 Hz, Ar-C*H*$_2$-Ar), 4.15–4.24 (m, 8H, Ar-O—C*H*$_2$), 4.47 (d, 4H, *J* = 13.0 Hz, Ar-C*H*$_2$-Ar), 7.04 (s, 8H, Ar-*H*), 7.66–7.70 (m, 60H, P-Ar-*H*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 24.72 [P^+], −143.39 [PF_6]. *m/z* (MALDI) 1447.60 $(M-PF_6)^+$. Anal. Calcd for $C_{132}H_{144}O_4P_4(PF_6)_4$: C, 63.46; H, 5.81. Found: C, 63.30; H, 5.78.

*Tetrakis-(4-(P,P-diphenyl-P-methylphosphonium)-butoxy)-p-tert-butylcalix[4]arene tetrabromide (**6**)*

Into a 100 cm^3 flask containing **S**$_5$ (1.184 g, 1.00 mmol) dissolved in chloroform (30 cm^3), diphenylmethylphosphine (4.004 g, 20.00 mmol) in chloroform (20 cm^3) was added. After 6 days under reflux, the mixture was cooled and the solvent was evaporated. The product was purified by precipitation from a 1:9 dichloromethane–hexane mixture to give compound **6** (1.190 g, 0.59 mmol) in 59% yield. Mp 160°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.03 (s, 36H, —C(C*H*$_3$)$_3$), 1.55–1.75 (m, 8H, —C*H*$_2$—CH$_2$—P), 2.30–2.48 (m, 8H, —C*H*$_2$—CH$_2$—O), 2.91 (d, 12H, *J* = 13.5 Hz, C*H*$_3$—P), 3.03 (d, 4H, *J* = 12.8 Hz, Ar-C*H*$_2$-Ar), 3.70–3.87 (m, 16H, —C*H*$_2$—P and C*H*$_2$—O), 4.26 (d, 4H, *J* = 12.8 Hz, Ar-C*H*$_2$-Ar), 6.71 (s, 8H, Ar-*H*), 7.54–7.78 (m, 24H, P-Ar-*H meta, para*), 8.02–8.17 (m, 16H, P-Ar-*H ortho*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 25.98. *m/z* (MALDI) 1909.68 $(M-Br)^+$. Anal. Calcd for $C_{112}H_{136}O_4P_4Br_4$: C, 67.61; H, 6.89. Found: C, 68.59; H, 7.10.

*Tetrakis-(4-(P,P-diphenyl-P-methylphosphonium)-butoxy)-p-tert-butylcalix[4]arene tetraperchlorate (**6a**)*

Compound **6a** was obtained according to the same procedure as for **5a** with **6** (0.100 g, 0.05 mmol) and $AgClO_4$ (0.050 g, 0.24 mmol) in 90% yield. Mp > 120°C decomposition. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.09 (s, 36H, —C(*CH*$_3$)$_3$), 1.65–1.80 (m, 8H, —*CH*$_2$—*CH*$_2$—*P*), 2.35–2.50 (m, 8H, —*CH*$_2$—CH$_2$—O), 2.50 (d, 12H, *J* = 12.0 Hz, *CH*$_3$—P), 3.18–3.28 (m, 8H, —*CH*$_2$—P), 3.38 (d, 4H, *J* = 12.8 Hz, Ar-*CH*$_2$-Ar), 4.15–4.28 (m, 8H, —*CH*$_2$—O), 4.45 (d, 4H, *J* = 12.8 Hz, Ar-*CH*$_2$-Ar), 6.97 (s, 8H, Ar-*H*), 7.60–7.87 (m, 40H, P-Ar-*H*, *ortho, meta, para*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 24.77. *m/z* (MALDI) 1966.24 $(M-ClO_4)^+$. Anal. Calcd for $C_{112}H_{136}O_4P_4(ClO_4)_4$: C, 65.05; H, 6.63. Found: C, 65.13; H, 6.72.

*Tetrakis-(4-(P,P-diphenyl-P-methylphosphonium)-butoxy)-p-tert-butylcalix[4]arene tetrahexafluorophosphate (**6b**)*

Compound **6b** was obtained according to the same procedure as for **5b** with **6** (0.100 g, 0.05 mmol) and $AgPF_6$ (0.069 g, 0.27 mmol) in 80% yield. Mp 155°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.11 (s, 36H, —C(*CH*$_3$)$_3$), 1.55–1.70 (m, 8H, —*CH*$_2$—CH$_2$—P), 2.24–2.38 (m, 8H, —*CH*$_2$—CH$_2$—O), 2.42 (d, 12H, *J* = 12.0 Hz, *CH*$_3$—P), 2.95–3.10 (m, 8H, —*CH*$_2$—P), 3.39 (d, 4H, *J* = 12.8 Hz, Ar-*CH*$_2$-Ar), 4.05–4.20 (m, 8H, —*CH*$_2$—O), 4.42 (d, 4H, *J* = 12.8 Hz, Ar-*CH*$_2$-Ar), 7.00 (s, 8H, Ar-*H*), 7.58–7.80 (m, 40H, P-Ar-*H*, *ortho, meta, para*). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 24.50 [P^+], −143.07 [PF_6], *m/z* (MALDI) 2104.80 $(M-PF_6)^+$. Anal. Calcd for $C_{112}H_{136}O_4P_4(PF_6)_4$: C, 59.79; H, 6.09. Found: C, 59.87; H, 6.03.

*Protonated tetrakis-(4-(P,P-diphenyl-phosphine)-butoxy)-p-tert-butylcalix[4]arene tetrabromide (**7**)*

Into a 50 cm^3 flask containing **S**$_6$ (1.510 g, 0.94 mmol) in dichloromethane (10 cm^3), HBr (5 cm^3; solution of 33%

wt. in glacial acetic acid) in dichloromethane (15 cm^3) was added. The mixture was left stirred for 24 h at room temperature. The mixture was then evaporated to give the pure product **7** (0.954 g, 0.49 mmol) in 52% yield. Mp 175°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.22 (s, 36H, —C(CH_3)$_3$), 1.80–2.15 (m, 16H, O—CH_2—CH_2—CH_2—CH_2—P), 2.92–3.10 (m, 4H, Ar-CH_2-Ar), 3.18–3.30 (m, 8H, CH_2—O), 3.40–3.55 (m, 8H, —CH_2—P), 4.05–4.27 (m, 4H, Ar-CH_2-Ar), 7.05 (s, 8H, Ar-*H*), 7.60–8.05 (m, 40H, P-Ar-*H*, *ortho, meta, para*), 10.30–10.40 (m, 4H, *H*-P). ^{31}P NMR (400 MHz, $CDCl_3$) δ (ppm): 46.32 [P^+]. *m/z* (MALDI) 1849.04 $(M-Br)^+$. Anal. Calcd for $C_{108}H_{128}O_4P_4Br_4$: C, 67.08; H, 6.67. Found: C, 66.84; H, 6.92.

NMR studies

Five milligrams of ligand were introduced with 6 equivalents of the solid alkali metal salts (Li^+, Na^+, Cs^+) or tetraethylammonium perchlorate in a glass vessel and dissolved in a small volume of deuterated chloroform or acetonitrile. After manual shaking for a few minutes, the mixture was left in contact for 24 h before filtration of the excess of salt, if necessary. The solution (or the filtrate) was then sampled in a NMR tube and its spectrum recorded on Bruker SY300 MHz or SY400 MHz spectrometers equipped for ^{1}H or ^{31}P resonances.

Microcalorimetric studies

Microcalorimetric titrations were performed using a 2277 Thermal Activity Monitor Microcalorimeter (Thermometric). Titration was carried out at 25°C on 2.7 cm^3 of 10^{-5} to 5×10^{-4} M solutions of the ligand in acetonitrile using a glass cell of 4 cm^3. The heat changes were measured after injection of 15×15 µl of 10^{-3} and 10^{-2} M $LiClO_4$, LiBr, $NaClO_4$, $NaPF_6$ or Et_4NClO_4 solutions in the same solvent. Chemical calibration was made by the determination of the complexation enthalpy of Ba^{2+} with 18C6 in water or of Rb^+ with 18C6 in methanol, as recommended (*37*). Values of the stability constants (β) and of the enthalpies of complexation (ΔH) were refined simultaneously from these data using the ligand-binding analysis program DIGITAM version 4.1 (*38*) and after correction for the heat of dilution determined in separate experiments by adding the salt solutions to 2.7 cm^3 of the pure solvent. The values of the corresponding entropies of complexation (ΔS) were then derived from the expressions $\Delta G = -RT \ln \beta$ and $\Delta G = \Delta H - T\Delta S$.

Ion-selective electrodes

THF was dried and freshly distilled before use for the preparation of the ion-selective membranes. PVC, *o*-NPOE, BEHS and (2-morpholino)ethanesulphonic acid monohydrate (MES) were obtained from Fluka Selectophore (Derbyshire, UK). The $LiClO_4$, $CsClO_4$ and sodium salts, Cl^-, Br^-, I^-, ClO_4^-, SCN^-, NO_3^-, SO_4^{2-}, CO_3^{2-}, HPO_4^{2-}, PO_4^{3-}, $Cr_2O_7^{2-}$, citrate, acetate, benzoate and oxalate, were of p.a. grade. All aqueous salt solutions were prepared with demineralised water (conductivity < 1.0 µS/cm).

The membranes were composed of 4 mg of ionophores **1**–**6** and **8**, 60 mg of PVC and 120 mg of plasticiser. All the components were dissolved in 1.5 cm^3 of dried, freshly distilled THF and the solutions were poured into glass rings of 24 mm in diameter. The solutions were left for 24 h for slow solvent evaporation giving the mother membranes of a thickness of about 0.1 mm. Several membranes of 7 mm in diameter were cut from each mother membrane and were incorporated into the Ag/AgCl electrode bodies of IS 561 type (Moeller SA, Zurich, Switzerland). The two plasticisers, BEHS and *o*-NPOE, were used for the preparation of the membranes. However, electrodes with membranes based on NPOE had the best lifetime and response characteristics. The EMF measurements were carried out at zero current conditions using a Lawson Lab 16 EMF station (multichannel millivoltmeter) or a Metrohm 654 millivoltmeter. A double-junction reference Radelkis 0P0820P electrode with a 1 M CH_3COOLi solution in the bridge cell was used. The measurements were carried out using cells of the type

Ag/AgCl|1 M KCl|1 M CH_3COOLi|sample|membrane|0.05 M MES/NaOH, 0.01 M NaCl|AgCl/Ag.

At least three identical electrodes of the same membrane composition and containing the same inner electrolyte were prepared (*39*). The studies were repeated several times over the period of 1 month.

To reduce the pH changes during the titrations, solutions were prepared with 0.05 M MES/NaOH buffer of pH 5.5 (MES). All salt solutions contained 10^{-2} M NaCl as the supporting electrolyte (*22*).

The selectivity coefficients $K^{pot}_{A,B}$ of the electrodes were determined by the separate solution method and in some cases by the fixed interference method (*40–42*). The calibration curves were obtained by the addition of standard

solutions of different anions to 50 cm^3 of 0.01 M NaCl in 0.05 M MES/NaOH buffer solution of pH 5.5. The concentration of the primary anion [A] was increased from 10^{-7} to 10^{-2} M. They were also measured by successive dilution of initial 5×10^{-2} M salt solutions until further dilution resulted in no potential change.

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